APPENDIX I: INTERNATIONAL REGULATION OF GENETICALLY MODIFIED MICROORGANISMS

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REGULATION OF GENETICALLY MODIFIED MICRO-ORGANISMS IN CANADA, JAPAN AND THE EUROPEAN COMMUNITIES

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1. INTRODUCTION

This report discusses regulations, comparable to the final EPA rule, applicable to genetically modified micro-organisms in Canada, Japan and the European Communities (EC), excluding their use in the areas of pharmaceuticals and pesticides. If included in the scope of the relevant regulations, other (micro-) organisms are addressed as well.

The analysis is based on the text of regulations, published and unpublished literature, interviews with officials and former officials of agencies in the respective countries and experts on biotechnology regulation, and personal knowledge of the authors. Since regulations are currently under development or review in all three areas investigated, a definitive description is not possible.

The evaluation of each of the relevant regulations includes wherever relevant:

- the depth and scope of regulatory review
- regulatory categories; commercial and R & D use
- notification, prior review and prohibition
- nature and amount of information requirements
- review time prior to commercial/research use.

The regulatory approaches in Canada, Japan and the EC are very different. This limits the possibility of comparative analysis of the respective legal schemes. The major differences are related to:

- the scope of regulatory review;
- formal vs. informal regulatory scrutiny;
- responses of industry to government and public opinion.

2. CANADA

2.1. INTRODUCTION

Regulatory requirements for biotechnology exist under a variety of product-oriented legislation. The main departments involved are Agriculture Canada, Environment Canada, and Health and Welfare Canada. Existing regulation and legislation of all types are being reviewed by these departments for their applicability to biotechnology to determine whether revisions are necessary. Other departments are also examining legislation which may be applicable to biotechnology. The Interdepartmental Committee on Biotechnology and its Sub-Group on Safety and Regulation serve to coordinate discussion of biotechnology regulation.

Most legislation applicable to biotechnology pertains to specific product categories, without regard to the process of production (i.e. whether biological or non-biological). The new Canadian Environmental Protection Act (outlined below) provides government authority to review and regulate potential risks of new biotechnology products not similarly reviewed under other legislation.

The Pest Control Products Act, administered by Agriculture Canada, is an important act for the regulation of genetically modified organisms. This Act requires registration of all microbial pest control products prior to the manufacture, sale or use in Canada. Guidelines under the Act address registration and field trial requirements for naturally occurring microbial pest control agents.

2.2. LABORATORY BIOSAFETY

Guidelines:

Laboratory Biosafety Guidelines, Medical Research Council of Canada and Health and Welfare Canada, 1990

Background:

The first version of these Guidelines was published in February 1977 by the Medical Research Council of Canada (MRC) as "Guidelines for the Handling of Recombinant DNA Molecules and Animal Viruses and Cells". Revisions took place in 1979 and 1980. The current version was issued jointly by the MRC and Health and Welfare Canada (HWC) in 1990.

Scope:

The Guidelines apply to the use of bacteria, viruses, parasites, fungi and other infectious agents which are pathogenic to man, in contained laboratory research (including university laboratories and hospitals and their affiliated institutions). Recombinant DNA microorganisms are included in the scope. The Guidelines do not apply to deliberate release or large scale research. What constitutes large scale research or deliberate release is not defined in the guidelines; recombinant DNA organisms are likewise not defined.

Initially, MRC issued the Guidelines because of its support of research in universities and their affiliated teaching hospitals. HWC made the Guidelines applicable to all research carried out or supported by the federal government. A number of provincial and private research funding agencies also adopted and implemented the Guidelines. The Guidelines apply to private institutions only

on a voluntary basis; many industries have adopted them. Environment Canada and Health and Welfare Canada recommend that the Guidelines be followed during all laboratory research.

Notification:

There are no notification requirements for laboratory research.

Levels of containment:

The Guidelines distinguish four risk groups of microorganisms, based on the degree of pathogenicity, and risk of infection and spread. For each of the groups, the various species which comprise that group are specifically listed.

- Group 1: low individual and community risk
- Group 2: moderate individual risk, limited community risk
- Group 3: high individual risk, low community risk
- Group 4: high individual risk, high community risk

There are four corresponding levels of physical containment.

2.3. USE OF GENETICALLY ENGINEERED MICROORGANISMS

2.3.1. The Canadian Environmental Protection Act

Background:

The Canadian Environmental Protection Act (CEPA), effective on June 30, 1988, was developed primarily to address issues involving chemical contaminants in the environment, including the regulation of new chemicals. The structure for the regulation of toxic substances is similar to that of the US TSCA. The CEPA provides the main statutory authority by which Environment Canada regulates biotechnology products.

CEPA is administered primarily by Environment Canada; Health and Welfare Canada has authority for requiring and evaluating human health information.

Relevant scope for genetically modified microorganisms:

Sections 25 to 32 of the Act provide for the assessment of potential effects on public health and the environment of "substances new to Canada", prior to manufacturing or importation. These review procedures apply to products created through biotechnological processes, as well as to chemicals.

Regulation of new substances under the CEPA may provide for information requirements, review periods, and test procedures and laboratory practices to be followed in developing test data. Any phase in the development of a product can be addressed in the regulations, from research through manufacture, use and transport to disposal, and prohibitions or conditions can be placed on particular products after assessment.

Substances regulated under any other act that provides for prior notification and assessment of toxicity, are exempted from the scope of the CEPA section on substances new to Canada. Accordingly pesticides, foods and pharmaceuticals, are excluded from the scope.

Products which could be regulated under the Act include naturally occurring and genetically engineered organisms. Applications affected by the Act include pollution degradation, waste disposal, mineral leaching, lignin degradation, and the production of chemicals.

Notification and review:

The CEPA section on substances new to Canada requires the compilation of a "Domestic Substances List", specifying all substances imported into, or manufactured, used, or traded in Canada in 1984-1986. Substances on this list are grandfathered under the regulations. Importation or manufacture of substances not on the Domestic Substances List is prohibited, unless certain information is provided and a certain period has expired. When no other review period is prescribed by regulation, a period of ninety days applies.

Regulations under the CEPA:

For the notifications, regulations may define substances and establish groups of substances; prescribe information requirements; review periods and review procedures; and make exemptions for certain quantities, conditions, uses or substances.

The notification schemes to be prescribed in the regulations can address commercial products as well as research activities in industry, universities and government.

2.3.2. Regulation of Biotechnology under CEPA (being drafted)

Background:

A proposal for the regulation of biotechnology under the CEPA, specifying information requirements and assessment procedures, is being drafted by Environment Canada and Health and Welfare Canada. The proposal may be expected later in 1990.

An earlier "Discussion Draft: Regulations Respecting Notification of Substances New to Canada", issued for comment in December 1987, is currently under substantial revision. The 1987 draft was felt to lack detail, and the new version will provide a more comprehensive system. Major items of controversy in the 1987 draft included the length of the assessment period, the scope of the definition of biotechnology product, and the potential involvement with research.

Scope:

The new draft proposal will include procedures for risk assessment by government prior to environmental release or commercial production of genetically engineered organisms (GEOs). The information requirements for such assessment are currently under development and will be circulated for comment within the next month or two. R & D involving GEOs which are already covered by other guidelines or regulations will be either exempted from the scope of the new regulations or subject to minimal requirements. A definition of GEOs has not yet been developed.

For large scale research, guidelines may be drafted, or existing ones adapted (the definition of large scale research has not yet been developed).

Review prior to environmental releases:

Government review of intended environmental release of GEOs will be undertaken in phases. Initial assessments will be required before small scale field trials on a case-by-case basis. The results of these tests will be evaluated by the government before large scale releases and commercial production may be carried out.

Exemptions:

For particular applications data submission may be waived in whole or in part (as was also envisioned in the 1987 draft regulations).

2.4. DELIBERATE RELEASES IN CANADA

No field tests with living recombinant DNA microorganisms have been undertaken yet. Earlier this year, a trial was undertaken involving the injection in plants of dead genetically engineered microorganisms.

Plasmid-cured and transconjugant Bacillus Thuringiensis strains have been field tested in Ontario and Quebec; approval was given case by case, on the basis of existing regulations applying to naturally occurring microbes.

Approvals for releases of several genetically modified plants have been granted since 1988.

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3. JAPAN

3.1. INTRODUCTION

Japan controls activities involving genetically modified organisms through guidelines from the executive branch of government rather than through legislation or regulations based on statutes. Each of the relevant ministries or agencies in Japan initiated the drafting of guidelines for its area of jurisdiction.

The Science and Technology Council (STC), established in the Prime Minister's Office, coordinates these activities, to prevent discrepancies in agency policies. Before a guideline is issued, it is reviewed by the STC, and disputes about jurisdiction or policy are dealt with in the STC. The administrative tasks of the Council are handled jointly by the Science and Technology Agency and the Ministry of Education, Science and Culture. The STC has a Committee on Life Science, which in turn has a Subcommittee on recombinant DNA.

While none of the guidelines has the force of law, government guidelines are accepted as binding by Japanese industry. There is an informal system of financial and social punitive action to which industry and laboratories are sensitive.

There is no significant opposition to the current advancement of biotechnology in Japan. This high level of public acceptance can also be noticed with respect to other high-technology developments. However, some interest groups question the safety and ethics of rapid advancement in biotechnology.

3.2. RECOMBINANT DNA RESEARCH

Guidelines:

Guidelines for Recombinant DNA Experiments, Prime Minister, September 16, 1987

Scope:

The guidelines apply to contained recombinant DNA research, whether privately or publicly funded. There is a formally separate set of guidelines with practically the same contents for universities, issued by the Ministry of Education, Science and Culture (MESC) in 1986, because the Prime Minister cannot issue guidelines which apply to university research funded through the MESC, for reasons of academic freedom.

The Japanese guidelines for recombinant DNA experiments are generally considered more stringent than the Guidelines of the National Institutes of Health in the US, entailing a more detailed internal review by the research organization (A.D. Little Report 1986, p.5; Uchida 1988, pp.255 f.).

Background:

In March 1979, the Ministry of Education, Science and Culture (MESC) adopted guidelines for recombinant DNA research at universities; a few months later, the Science and Technology Agency (STA) proclaimed similar guidelines for research at government and private institutions. Both sets of guidelines have been revised several times. In 1983, a revision drafted by the Life Science Committee of the Council for Science and Technology was made applicable to

industrial, government and university recombinant DNA research. The last revision of these guidelines was proclaimed in September 1987 by the Prime Minister. A new revision is currently in preparation.

Containment levels:

The Guidelines distinguish seven physical and two biological containment levels.

For small-scale experiments (less than twenty liters), there are four physical containment levels: P1 to P4. However, P4 research has never taken place in Japan. For each of the containment levels, prescriptions are given for three aspects: "containment equipment", "special laboratory design", and "laboratory practices".

For large scale applications, there are three physical containment levels: LS-C, LS-1, and LS-2. Large-scale experiments are recombinant DNA experiments in which the volume of culture solution handled exceeds 20 liters. Prescriptions are given for "containment facilities and their design" and for "laboratory practices".

Besides these physical means of control there are two levels of biological containment, B1 and B2, based on the degree of safety of the host-vector systems.

Notification:

There is neither a general notification requirement, nor a government review system for the experiments under the guidelines. Certain experiments, such as those conducted at the LS-C level, require "government supervision". The Guidelines do not define or clarify what government supervision entails. The responsibility for supervising the research is delegated to the STA, except for university research funded through the MESC.

Prior review and classification into containment levels:

Prior to the commencement of experiments a safety assessment is performed by the research laboratory on which basis the proper physical and biological containment levels are selected. Heads of research institutions assume responsibility for the safety of experiments performed by researchers at their institution. They approve or disapprove individual planned experiments. A Safety Committee, which has to be established at each research institution engaged in recombinant DNA research, advises the head of the institution on the acceptability of planned experiments.

The safety assessment focuses, where relevant, on issues such as the biological characteristics of the DNA donor cells, the newly acquired characteristics of the host after DNA insertion, the purity of the DNAs, the number of clones, and the culture scale.

LS-1 and LS-2 containment criteria are to be applied to experiments which would have called for P1 and P2 levels respectively, if carried out on a smaller scale. If the rDNA organisms are "verified" as extremely safe, the experiments may be conducted "under government supervision" at the LS-C level or with "special methods of containment" which are not included in one of the three LS levels.

Prohibitions:

Experiments which go beyond those categorized in the guidelines are to be conducted "under the direction of the government". The Guidelines do not define or clarify what government direction entails. Examples include

- the use of host-vector systems other than those allowed for the B1 and B2 biological containment levels;
- cloning experiments of genes for the biosynthesis of toxic molecules lethal for vertebrates;
- experiments in which recombinant DNA organisms infect plants or animals;
- large scale experiments at the P3 or P4 physical containment level; and
- deliberate release of recombinant DNA organisms into the environment.

Under the Guidelines, deliberate release may only be conducted under the direction of the government. The Guidelines do not contain provisions for prior review. No field tests have yet taken place.

Additional features:

The guidelines stress the individual responsibility and the necessity of continued training of researchers and laboratory supervisors. Laboratory supervisors and heads of research institutions are to be held explicitly responsible for knowledge of relevant rules and safety techniques and training of personnel. Research institutions are obliged to have a Safety Committee and a Safety Officer. For work with pathogenic microorganisms, medical screening is required.

3.3. INDUSTRIAL APPLICATIONS

Guidelines:

Guideline[s] for Industrial Application of Recombinant DNA Technology, Ministry of International Trade and Industry (MITI), June 19, 1986

Scope:

The guidelines apply to the use of recombinant DNA technology in industrial processes. They focus on various industrial applications, including manufacturing and mining, but do not apply to agricultural or other environmental use of genetically modified organisms.

Background:

The Guidelines were drafted by a subcommittee of the Chemical Products Study Council, chaired by Prof. Hisao Uchida (Tokyo University), in 1984-1986. They fully adhere to the recommendations of the 1986 OECD report "Recombinant DNA Safety Considerations".

Classification into safety categories:

The "person in charge of a working organization" is responsible for the evaluation of the safety of recombinant DNA organisms to be used in industrial processes. Relevant "items for evaluation" may include the taxonomy, genetic characteristics, and pathogenic and physiological traits of the recipient organism, the construction and the method of construction of the recombinant DNA molecule, the properties of DNA donor and vector donor, the gene expression characteristics of the recombinant DNA organism, and the similarity of the recipient organism and the recombinant DNA organism.

Based on this evaluation, the same person classifies the recombinant DNA organisms into one of following safety categories:

- GILSP (Good Industrial Large Scale Practice);
- Category 1 (non-pathogenic organisms not included in GILSP);
- Category 2 (pathogenic; infections will not result in a serious outbreak);
- Category 3 (pathogenic organisms not included in Category 2).
- Recipient organisms which might be "significantly harmful to human health", and result in a disease for which no effective preventive nor therapeutic method is known, are to be assigned a classification separate from Category 3, and treated in a "special manner".

Each of the categories have corresponding rules of operation for cleaning and maintenance of equipment and apparatuses; hygiene of personnel; and inoculation, transfer, sampling, waste treatment, storage, and transportation of organisms.

Notification and prior review:

None of the applications under the guidelines require mandatory notification or prior review by the government. In order to secure safety, the organizer of a working organization can request MITI to confirm that his equipment, apparatuses, operations and management are in accordance with the guidelines. In the first two years of the existence of the guidelines MITI has authorized 114 industrial applications in this way.

3.4. AGRO-INDUSTRIAL APPLICATIONS

Guidelines:

Guidelines for the Application of Recombinant DNA Organisms in Agriculture, Forestry, the Food Industry and other Related Industries in Japan, Ministry of Agriculture, Forestry and Fisheries (MAFF), December 18, 1986

Scope:

The guidelines apply to agro-industrial use of recombinant DNA (rDNA) organisms. Their purpose is "to promote the progress of agro-industries by defining general principles for the appropriate application of rDNA organisms [...] and ensuring safety in the use of rDNA organisms".

Background:

The guidelines follow the 1986 OECD Recommendations.

Safety levels:

Recombinant DNA microorganisms for production processes are to be classified into five divisions according to the degree of safety required:

- GILSP (Good Industrial Large Scale Practice; minimum containment level)
- Category 1 (nonpathogenic microorganisms which cannot meet the criteria for GILSP)
- Category 2 (possibility of infection; minimal likelihood of pathogenicity)
- Category 3 (significant likelihood of pathogenicity to humans)
- Special class (very pathogenic)

For each of these categories there are prescriptions for use and conditions of facilities, apparatus and operations, management system and reporting.

For rDNA microorganisms, the points-to-consider for the determination of safety level include the purpose of the application, characteristics of hosts, donor DNA, and vectors, methods of preparation, expression of target genes, propagation style, pathogenicity, survivability, and monitoring methods.

Prior review and classification in safety levels:

A person who intends to produce, sell, or use rDNA organisms in agro-industries, is obliged to evaluate the characteristics and safety of the organisms, and apply the appropriate safety measures as outlined in the guidelines.

Notification:

The responsible person may, at his option, ask the Minister of Agriculture, Forestry and Fisheries to approve the facilities, apparatus and procedures developed for the application of rDNA organisms.

The responsible person is obliged to collect information on the rDNA organisms and their application, and to report immediately to the Minister any new knowledge that could influence the safety evaluation of organisms.

Review prior to deliberate release:

Prior to the application of rDNA organisms in the environment, the safety of the proposed application has to be "confirmed" through evaluation in a "simulated model environment". Under the Guidelines, only rDNA microorganisms classified under GILSP or Category 1 may be tested.

For rDNA microorganisms the simulated model environment is a "specifically restricted area under such conditions as to minimize both the spread of rDNA microorganisms outside the area and the transmission of the genetic characteristics of rDNA microorganisms to organisms outside this area. [...] An isolated field must be marked off or a management facility to prevent spread of rDNA microorganisms must be set up in the work area taking into consideration the propagation style, the restriction treatment for propagation ability, the physiological characteristics and the situation of application in the noncontained system of rDNA microorganisms as well as the surrounding biota."

3.5. APPROVALS FOR DELIBERATE RELEASES OF MICROORGANISMS

No deliberate releases of genetically altered organisms into the environment have taken place. None is pending or under review. However, field tests are expected in the near future in the areas of agriculture and environmental conservation.

3.6. FUTURE DEVELOPMENTS

MITI has announced that guidelines are being developed for application of genetically modified organisms in non-closed systems. MITI has been studying monitoring methods for [detecting deliberate release in] environmental applications for four years.

The Japanese Environmental Agency is concerned primarily with the deliberate release of microorganisms for application as biopesticides. It is anticipated that safety guidelines will be issued later in 1990.

Revisions of all of the guidelines discussed above are currently being prepared.

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4. THE EUROPEAN COMMUNITIES

4.1. INTRODUCTION

The Council of the European Communities (EC) has adopted two Directives to harmonize the regulation of the use of genetically modified organisms for the area of the EC. Present members of the EC are: Belgium, Denmark, the Federal Republic of Germany, France, Greece, Ireland, Italy, Luxembourg, the Netherlands, Portugal, Spain, and the United Kingdom.

A Directive is binding upon each member state as to the result to be achieved, but leaves to the national authorities the choice of form and methods (art. 189 of the EEC Treaty). Directives are adopted by the Council of the EC upon proposal of the Commission and in cooperation with the European Parliament. Following adoption by the Council, member states are obliged to implement Directives in their own legal system before a certain date specified in the Directive. Often, Directives prescribe a period of eighteen months for implementation by the member states. It is only after these implementations that the rules become effective in the respective member states.

The proposed Directives require every member state to designate a competent authority (CA). These CAs will receive and evaluate notifications of intended use of genetically modified (micro)organisms, and will be responsible for carrying out the provisions of the Directives. The compositions of these authorities as well as their positions in the national administrations fall within the discretion of the member states.

4.2. REGISTRATION OF RECOMBINANT DNA EXPERIMENTS

Council Recommendation:

"Recommendation Concerning the Registration of Work Involving Recombinant Deoxyribosenucleic Acid", Council of the European Communities, Recommendation 82/472/EEC, Official Journal of the European Communities No. L 213 of 21 July 1982, pp. 15 f.

Scope:

The member states were advised to establish a notification procedure for the registration of laboratories wishing to undertake work involving recombinant DNA techniques.

Notification:

It was recommended that the notification requirements include contemplated research projects, safety evaluations of these projects, descriptions of protective and control measures to be applied, and descriptions of the training in recombinant DNA work of those concerned with the execution, supervision, monitoring or safety of the individual experiments.

Implementation:

In 1983, the degree of implementation of the Recommendation in the member states was studied by means of a questionnaire. The answers [as outlined in EC Commission document BRIC/1/86 (1986)] indicated the following:

- the United Kingdom and Denmark were the only two member states where a system of notification had been rendered compulsory for all laboratories;
- in the Federal Republic of Germany notification was compulsory for research work supported by the government. Research not funded by the federal government was under a system of voluntary registration;
- in Belgium, France, Greece, Ireland and the Netherlands, research laboratories were asked to register voluntarily;
- Italy was preparing safety regulations, compatible with the terms of the recommendation;
- Ireland had adopted a definition of recombinant DNA work which differed from that in the recommendation.

4.3. CONTAINED USE

Council Directive:

"Council Directive of 23 April 1990 on the Contained Use of Genetically Modified Microorganisms," Directive 90/219/EEC, Official Journal of the European Communities No. L 117 of 8 May 1990, pp. 1-14.

Background:

The initial proposal for a Directive [document COM(88)160] was presented by the Commission to the Council on 4 May 1988. The European Parliament (EP) delivered its opinion on 24 May 1989. The Commission amended its proposal, taking the opinion of the EP into account [document COM(89)409, August 1989]. On 23 April 1990, the Council adopted the Directive.

Implementation:

The member states have to bring into force the laws, regulations and administrative provisions necessary to comply with the Directive before October 23, 1991.

Scope:

All the contained uses of genetically modified microorganisms (GMMOs), i.e. small-scale as well as large scale.

Genetic modification includes recombinant DNA techniques, as well as micro-injection, macro-injection, micro-encapsulation and cell fusion. Techniques of genetic modification to be excluded from the scope of the Directive [as listed in annex IB to the proposed Directive] are:

- mutagenesis,
- somatic animal hybridoma cells,
- cell fusion of cells from plants which can be produced by traditional breeding methods, and
- "self cloning of non-pathogenic naturally occurring micro-organisms which fulfill the criteria of the Group I containment category for recipient organisms".

The Directive does not apply to the storage, transport, destruction or disposal of GMMOs which have been placed on the market under EC legislation.

Containment levels:

The Directive classifies GMMOs in two categories, Group I and Group II. Group I is the lower risk category. Criteria for classification in Group I are provided in Annex II to the Directive. GMMOs which do not meet the criteria for Group I belong to Group II.

The classification criteria are related to characteristics of the recipient or parental organism, the vector or insert, and the GMMOs, and include factors such as pathogenicity, safety history, biological containment (survivability and replicability), mobility, and transfer of resistance markers.

With respect to culture volume and industrial use, the Directive distinguishes two types of operations, Type A and Type B. Type A operation is "any operation used for teaching, research, development, or non-industrial or non-commercial purposes and which is of a small scale (e.g. 10 liters culture volume or less)." All other operations are Type B.

Prior risk assessment by the user:

The user of the genetically modified organisms must carry out a prior assessment as regards the biological risks, and a record of this assessment must be kept. Annex III to the proposed Directive lists "safety assessment parameters" to be taken into account, which are divided into four categories:

- characteristics of the donor, recipient or (where appropriate) parental organisms;
- characteristics of the modified microorganisms;
- health considerations;
- environmental considerations.

Notification of first-time use of installations:

When a particular installation is to be used for the first time for operations involving the contained use of GMMOs, the user must submit a notification to the "Competent Authority" (CA) of the member state. Separate notifications must be made for the first use of Group I GMMOs and for the first use of Group II GMMOs in a particular installation (See Table 1).

The first-time use of an installation involving Group I GMMOs may proceed 90 days after the notification in the absence of a prohibition by the CA, or earlier with the agreement of the CA. The first-time use of an installation for Group II GMMOs requires explicit consent of the CA. The CA will take its decision within 90 days.

Notification of subsequent use:

A notification is required each time a particular Group I GMMO is used for the first time in a quantity over ten liters in an installation which previously has been approved for the use of Group I GMMOs. The use may proceed 60 days after the notification in the absence of a prohibition by the CA, or earlier with the agreement of the CA.

For Group II GMMOs, first use of a particular GMMO, in an installation which previously has been approved for Group II, must be notified for any quantity. Use in quantities under ten liters may proceed after 60 days if not prohibited by the CA. Use in quantities over ten liters may not commence before the CA has given its explicit consent. The CA will take its decision within 90 days.

Table 1 clarifies the notification procedures.

Table 1. Proposed Reporting for Contained Applications	
First use of particular installation for Group I GMMOs	- prior notification - use after 90 days if not prohibited
First use of particular installation for Group II GMMOs	- prior notification - explicit consent required - CA decides within 90 days
Type A use of Group I GMMOs in previously approved installation	- no notification required - records must be kept
Type A use of Group I GMMOs or Type B use of Group II GMMOs in previously approved installation	- prior notification - use after 60 days if not prohibited
Type B use of Group II GMMOs in previously approved installation	- prior notification - explicit consent required - CA decides within 90 days

Information requirements for notifications:

Annex V to the proposed Directive clarifies the information requirements for Group I and Group II GMMOs for quantities under and over ten liters.

Review by the CA:

The Competent Authority examines the accuracy and completeness of the information given in the notification, the correctness of the classification, and, where appropriate, the adequacy of the waste management, safety, and emergency response measures. The Competent Authority may ask for further information prior to the proposed use, or subject the use to certain specific conditions.

Periods of time during which the CA awaits additional information which it has requested from the notifier, or during which a public enquiry is being carried out, are not taken into consideration in these periods.

Additional features:

The Directive contains provisions regarding emergency response measures, inspections and confidential treatment of information.

4.4. DELIBERATE RELEASE

Council Directive:

"Council Directive of 23 April 1990 on the Deliberate Release into the Environment of Genetically Modified Organisms", Directive 90/220/EEC, Official Journal of the European Communities, No. L 117 of 8 May 1990, pp.15-26.

Background:

The initial proposal for a Directive [document COM(88)160] was presented by the Commission to the Council on 4 May 1988. The European Parliament (EP) delivered its opinion on 25 May 1989, proposing 17 amendments. The Commission amended its proposal, taking the opinion of the EP into account, and incorporating ten of the proposed amendments [document COM(89)408]. On 30 November 1989, the Council adopted a "Common Position" with a view to the adoption of the Directive, incorporating most of the text of the proposal (document 9644/89), and on 23 April 1990, the Directive was adopted

Implementation:

The member states have to bring into force the laws, regulations and administrative provisions necessary to comply with the Directive before October 23, 1991.

Scope:

Deliberate releases of genetically modified organisms (GMOs) into the environment. The proposed Directive seeks to establish two different procedures: one for experimental releases, where each Competent Authority is fully responsible for the releases carried out in its member state, and a second for the placing on the market of genetically modified organisms for a given use, where agreement with the other member states is needed before the product may be endorsed.

The second procedure does not apply to products covered by EC legislation which provide for an environmental risk assessment procedure similar to that of the Directive.

The proposed Directive does not apply to transport of GMOs.

Prohibitions:

No release of GMOs which falls within the scope of the Directive may be carried out before a Competent Authority has given its consent.

4.4.1. Releases for R & D Purposes

Notification:

The Directive establishes a case-by-case notification and endorsement procedure. Before carrying out a release, the person responsible for it must submit a notification to the CA of the member state within whose territory the release is to take place. This notification has to include a technical dossier supplying information necessary for risk evaluation and a statement evaluating the impacts and risks for human health and the environment.

Prior review:

The CA is to review and evaluate the notifications and to decide upon consent, conditions of the release, requirement of additional information, or rejection. The CA responds within 90 days after notification. See Table 2. Periods of time during which the CA awaits additional information which it has requested from the notifier, or during which a public enquiry is being carried out, are not taken into consideration in the 90 day-period.

Tests or inspections may be carried out for control purposes.

Additional features:

Where a member state considers it appropriate, it may provide that certain groups or the public be consulted.

After completion of the release, the notifier is required to send the CA a risk evaluation report.

The Commission of the EC will establish a system for the exchange of information between the CAs of the member states.

4.4.2. Placing Products Containing GMOs on the Market

Notification:

The manufacturer or importer is required to submit a notification to the CA of the member state in which he wants to place a certain product on the market for the first time.

This notification must contain a technical dossier and a risk impact statement (as in the case of R & D purposes), taking into account the diversity of sites of release, uses of the product and results known from releases in other countries.

In addition, supplementary information is required, in particular specific conditions of use and handling and a proposal for labelling and packaging; Annex III to the Directive clarifies these requirements.

Prior review:

Within 90 days (waiting time for additional information excluded), the CA either sends the dossier to the Commission of the EC with a favorable opinion, or rejects the proposal.

The Commission forwards the dossier to the CAs of the other member states. If no member state raises an objection within 60 days after distribution of the dossiers, the CA which was notified gives its written consent, and informs the other member states and the Commission thereof. See Table 2. If any objection is raised, and the CAs cannot reach an agreement, the Commission shall make the decision, assisted by a Committee composed of member states representatives. When the Commission takes a favorable decision, the CA that received the original notification is required to give its consent.

Once a product has received a written consent, it may be used throughout the EC without further restrictions, under the conditions for use and geographical areas stipulated in the consent.

Table 2. Proposed Reporting for Deliberate Release	
Releases for R & D Purposes	- prior notification - explicit consent required of CA in relevant member state - CA decides within 90 days
Marketing of GMOs	- prior notification - notified CA decides within 90 days, than sends dossier to other CAs for 60 day review - explicit consent required of CA to whom notified; any CA may raise objections; if the CAs cannot reach agreement, the Commission decides

Additional features:

When a member state has "justifiable reasons" to consider that a product on the market constitutes a risk, it may provisionally restrict or prohibit its use and/or sale.

4.5. REGULATION IN EC MEMBER STATES

At present, environmental regulation of biotechnology differs rather drastically in the various countries which form the EC. The approaches vary from complete absence of specific regulations, to guidelines applied on a voluntary basis, to comprehensive legislation. Of course, in practically all member states a variety of health and environmental protection laws are applicable to genetic engineering, in part enacted to regulate the 'old' biotechnology. The scope of these older laws is normally limited to worker protection and the commercialization of products.

In Greece, Italy, Luxembourg, Portugal and Spain, there are no specific regulations with respect to applications of genetic engineering. Under the new EC Directives, these countries are obliged to develop licensing systems before October 23, 1991.

Other European countries have adopted guidelines or regulations. Most countries have guidelines for recombinant DNA research, based upon the Guidelines of the NIH. These guidelines are to be applied voluntarily in most cases. The United Kingdom and Denmark have adopted mandatory guidelines; in the Federal Republic of Germany the guidelines applied are either mandatory or voluntary depending on the funding of the research.

4.5.1. Regulation in the United Kingdom

New Genetic Manipulation Regulations (1989 No.1810), issued under the Health and Safety at Work Act 1974, came into force in the UK in November 1989. The Regulations introduced mandatory notification of the use of genetically manipulated organisms (GMOs) and of the intentional introduction of such organisms into the environment.

Under the Regulations, notification to the Health and Safety Executive (HSE) is required 30 days prior to the contained use of GMOs or 90 days prior to deliberate release. Responses from the HSE are given after consultation with the Advisory Committee on Genetic Manipulation (ACGM), which consist of employee representatives and medical and scientific experts. In addition to provisions for notification, the Regulations require assessment of risk by a method approved by the HSE and the establishment of a genetic manipulation safety committee at each center undertaking such work.

Mandatory requirements to notify laboratory work involving genetic manipulation continue to exist.

There have been several deliberate releases of GMMOs in the UK.

4.5.2. The Regulatory Approach in France

France has operated an oversight system for biotechnology on a case-by-case basis which has attracted very little opposition. There are no specific regulations for biotechnology. The French attitude is that existing regulations are sufficient to ensure safety. The French administrative system features a complicated network of committees operating in different ministries with responsibilities in the various steps from biotechnology research to the marketing of products. Acceptance of the proposed EC Directives will oblige France to adopt regulations implementing a specific review structure for biotechnology.

A relatively permissive attitude towards deliberate release has made France one of the leading locations for field tests. Out of 63 field tests conducted in 1987-1988, 19 took place in France, compared with 26 in the US, five in Belgium and four in the UK. Of the 19 French field trials, 17 involved plants, one test was carried out with microorganisms, and one with a vaccine (AGROW No.98, November 3, 1989, p.8).

4.5.3. Regulatory Developments in West Germany

In the Federal Republic of Germany, a commission ("Enquete Kommission") of the parliament ("Bundestag") issued the report Prospects and Risks of Genetic Engineering ("Chancen und Risiken der Gentechnologie") in January 1987. A section of the report examines the adequacy of existing laws that pertain to biotechnology. The report recommended that the existing guidelines for recombinant DNA research be made mandatory for all research, and a five-year moratorium be imposed on the deliberate release of genetically modified micro-organisms, from which exemptions would be possible on a case-by-case basis. The German parliament rejected the moratorium in October 1989.

In August 1989, a Genetic Engineering Law ("Gentechnik Gesetz") was proposed. This Act, in line with the proposed EC Directives, would legislate the use of genetically engineered organisms and the marketing of products containing such organisms. One of the features of the proposed Act is the establishment of mandatory review procedures for all deliberate releases.

In November 1989, a decision of the Administrative Supreme Court of the state Hesse forbade the industrial application of genetically engineered organisms, on the ground that there is no legal basis for such application. This ruling obliged the company Hoechst to stop the construction of an almost finished facility. This decision put pressure on the government to pass the Genetic Engineering Law as soon as possible. In April 1990, a revised version of the Law was approved in the lower chamber of the parliament, and passed for discussion to the upper chamber.

In the meantime, in the Fall of 1989, the Max Planck Institute for Plant Breeding Research in Cologne was granted the first exemption of the Recombinant DNA Guidelines for a field test of transgenic petunias in a fenced field at the Institute.

4.5.4. Denmark

Denmark was the world's first country to proclaim a statute regulating environmental application of biotechnology. This Environment and Gene Technology Act ("Lov om Miljø og Gensplejsning") came into force in June 1986. The Act establishes a licensing system for the development of biotechnology-derived products, which includes a procedure for risk assessment and inspection. Deliberate release of genetically engineered organisms is in principle prohibited. However, the Minister of the Environment may approve releases in "special cases". Before such an exemption is given, an assessment is to be made of the possible harmful effects on the environment (on a case by case basis). Detailed conditions may be prescribed for individual releases.

No genetically engineered microorganisms have been authorized for release as of October 1989.

4.5.5. Harmonization of Biotechnology Regulation in the EC

The four country descriptions provided above illustrate the intrinsically different approaches member states currently have with respect to biotechnology regulation. Implementation of the EC Directives will achieve a greater degree of uniformity. This is particularly true with respect to marketing of genetically modified organisms, because the CAs in all member states have to agree on the approval of marketing permits. Attitudes towards biotechnology will continue to play a role in the issuance of permits for contained use and field tests.

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